

**The Korean Intellectual Property Office (KR)
Publication of Application (A)**

**(51) Int.CI.
A61K 35/78**

(11) Publication No	10-2004-0052398		
(43) Publication Date	2004-06-23		
(21) Application No	10-2002-0080590		
(22) Application Date	2002-12-17		
(74) Agent	Dong-In Shin	(72) Inventor	Dong-U Kim Won-Guk Moon
(71) Applicant	EnBalOTeKeuNolReoJi CO., LTD Dong-U Kim Won-Guk Moon		

Examination Requested : Requested

(54) COMPOSITION COMPRISING THE EXTRACT OF GRAPE SEED HAVING A-GLUCOSIDASE INHIBITORY ACTIVITY, THE PREPARATION METHOD AND THE USE THEREOF

 **Abstract**

Machine Translation

Human Translation

1

The present invention relates to a composition and the sampling method containing the extract of grape seed in which it has the decrease of blood glucose effect and is to provide an economic, the grape seed water extracts or the health promoting food and the drug having the excel effect that hinders the action of the alpha glucosidase which is the ferment which is essential as to the carbohydrate digestive absorption of the animal and suppresses the absorption of the internal glucose and controlling after dinner blood sugar and the ethanol extraction material is effective for the prevention for adult chronic disease and treatment including the diabetes, the obesity suppression etc. it is not necessary to have the step of heating amount of the used organic solvent as to the method, for manufacturing an extract it controls a pH it adds the water to the grape seed is relatively small.

 **Representative Drawing(s)**

Fig. 1

 **Keyword(s)**

The grape seed, extract, alpha glucosidase inhibitor, blood sugar, diabetes, adult disease, health promoting food, drug.

 **Description**

► **Brief explanation of the drawing**

- 2 Fig. 1 is a graph showing about alpha amylase impediment of the spittle of the grape seed water extracts.
- 3 Fig. 2 is the graph showing about alpha amylase impediment of the pancreas of the grape seed water extract
- 4 Fig. 3 is a graph showing the enzyme reaction velocity about alpha-glucosidase impediment of the spittle the of the starch which is a concentration and substrate of the grape seed water extracts is differentiated.
- 5 Fig. 4 is a graph showing the enzyme reaction velocity about alpha-glucosidase impediment of the pancreas i content of the starch which is a concentration and substrate of the grape seed water extracts is differentiated.

► **Details of the Invention**

► **Purpose of the Invention**

The Technical Field to which the Invention Belongs and the Prior Art in that Filed

- 6 The present invention relates to the composition containing the extract of grape seed having the alpha-glucos inhibitory activity, and the manufacturing method and use. More concretely, it relates to the composition supp the hydrolysis of essential alpha-glucosidase enzymes and contains the extract of grape seed in which has th decrease of blood glucose, and the obesity inhibition effect in the carbohydrate metabolism and a method of manufacture thereof and use.
- 7 In the Bon-Cho-Gang-Mok of the eddy gin, the grape seed controls the arthritis of the bone and tendon and it enhances a radical and the grapes counts the power. And it firmly depends and it healthily does as a favor. M it had the effect of the etc. which made strong against a coiling while giving the patience tolerating a hunger. Therefore, if the grape was long eaten, a condition became lighter and a condition did not grow old, it could b
- 8 As described above, cities and provinces to develop the extract of the grape seed with a superior physiologic as the functional food or the therapeutic agent etc. are actively made. And the functional food containing the grape seed of the pee etc. which is coated with the extract of grape seed in the grape seed extraction native to the decayed tooth, and KR PT 01-12238 is disclosed in KR PT 98-51189 in the extract of grape seed as the tyros inhibition agent, and KR00-18117 B. And it discloses about use toward the antioxidation effect of the proanthocyanidin which is the main component of the extract of grape seed including the manufacturing method of the grapes p in which the antioxidant effect is improved in KR PT 00-63265 in the grapefruit seed oil in which an antioxidant contained and a method of manufacture thereof, and KR PT 01-04553 a medicine etc. a procyanidin in KR PT 28877 to the effective component. But as to a convention, the extract of grape seed hinders the action of an α glucosidase and the action is disclosed that it has the decrease of blood glucose effect.
- 9 The carbohydrate included among the food is disassembled to the monosaccharide like the glucose with the various alpha-glucosidases like the alpha amylase, isomaltase, glucoamylase, sucrase and the carbohydrate among the food is absorbed within the blood. Therefore, if the action of such alpha-glucosidase is hindered, s carbohydrate is unable to be disassembled to a monosaccharide, a carbohydrate is unable to be absorbed wi blood. Therefore, the sudden rising of the glucose density is supressed within the blood caused in the ingestio hydrocarbon.
- 10 That is, the α- glucosidase has the function of cutting the per within the polysaccharide and per, and the Glyc bond between a per and the lipid or the per and protein in a cell. And in case of hindering the glucosidase enz

reaction, the absorption of a per is delayed in the small intestine and it is effective for the diabetes and adipos treatment.

- 11 Therefore, many research toward the action inhibitor of the essential alpha-glucosidase enzyme had been be accomplished of the purpose of making use of the decrease of blood glucose adjustment in the carbohydrate metabolism. Consequently, oligostatin [Itoh J. et al.: J. Antibiotics,34, pp1424-1435, 1981]s obtained from the fluid of the soil actinomycetes, *** statin (trestatin) [Yokose K. et al.: J. Antibiotics,36,pp1157-1162, 1983] etc. reported. Acarbose [Schmidt D.D. et al.: Naturwis senschaften,64,pp535-538, 1977]s were discovered in the Bayer corp. at 1977 year and this was developed as the diabetes and obesity therapeutic agent. Besides, pre a restriction to the Japanese, the Vallee auramine (baliolamine) the clinical test about the deoxynojirimycin (deoxynojirimycin) leading chain miglitol is performed in the Germany Bayer [Foelsch U.R. et al.: Structure an Function of the small intestine: Caspyry W.F. et al.: Excerptamica, Amsterdam, pp310-318, 1987].
- 12 The till now many Diabetes cure of a kind was unable to be developed and an on-the-fly, the fixing method, o which it was satisfied the development is unable to be developed. There can be the method for directly admir the insulin to the insulin dependent patient or administering the sulfonylurea system derivative to the insulin independence patient and controlling the concentration of the glucose within the blood as the conventional fix method. But it has the problem of causing the edema of the skin due to the repeated Cinnabaritis as to a patient need the Cinnabaritis which the insulin can raise the side effect including the allergic reaction etc., and is regul long time because it cannot administer to an oral since being destroyed in the alimentary canal before reachir blood flow and the Cinnabaritis zero is used. And the sulfonylurea (sulfonyl urea) system drug including the tol (tolbutamide), the gliquidone etc can cause the hypoglycemia in the parallel use including the chloramphenicks blocking agent, the sulfa drug etc. And the biguanide (biguanide) system drug including the metformin etc. ha problem of causing the lactic acid excess etc. in the alcohol and parallel use.
- 13 Therefore, the problem of the method for controlling the glucose density within the conventional blood is over. The new method recently for preventing the absorption itself within the blood of the glucose is tried out. It is a as one among the new method as described above to develop alpha-glucosidase inhibitors as the Diabetes c glucosidase inhibitor can be used as a treatment and prevention including the adiposity and notice circumsta evidence etc. besides the diabetes since suppressing the glucose absorption itself within the blood.
- 14 As to these inventors, while searching the alpha-glucosidase inhibitor in the natural product in order to overcc problem including the side effect of conventional therapeutic agents etc., it discovered for the first time that it effect that the extract of grape seed suppressed an alpha-glucosidase. It completed the invention which these sampling methods freshly developed.

Technical challenges of the Invention

- 15 Therefore, an object of the present invention are to provide the composition for the decrease of blood glucose manufacturing the extract of grape seed with the new sampling method and has the extract of grape seed in \ the alpha-glucosidase inhibitory activity as the effective component or the diabetes or the treatment of obesity
- 16 ▶ Structure & Operation of the Invention
Above statement, to accomplish the above objects. And the present invention is to provide the composition fo decrease of blood glucose which it has the extract of grape seed in which it has the alpha-glucosidase inhibi activity as the effective component, it does.
- 17 The extract of grape seed provides the extract extracted from the grape seed of the grapes (*Vitis vinifera L.*),

European grape (*Vitis vinifera*), the *Vitis labrusca*, the *Vitis riparia*, the desert pavement (*Vitis rupestris*), the *V. berladieri*, the *Vitis coignetiae PULLIAT* (*Vitis coignetiae Pulliat ex Planchon*), the *Vitis amurensis Ruprecht*, the *Vitis flexuosa Bunge*, the *Vitis flexuosa THUNB* (*Vitis flexuosa Thunb.*) etc.

- 18 The extract of grape seed means the extract which is available in the polar solvent and these mixed solvents the water, a methanol, the ethanol etc.
- 19 Moreover, the present invention is to provide the diabetes, containing the extract of grape seed the obesity pr and for treating pharmaceutical composition.
- 20 Moreover, the present invention is to provide the method for manufacturing the extract of grape seed.
- 21 Below, and the present invention are more circumstantially illustrated.
- 22 The grape seed water extracts of the present invention provides the manufacturing method of the extract of g seed dry with (a) and including the manufacturing process consisting of the volume of 20 times through the *V* of the grape seed weight (kg) smashed, 50°C through 20 preferably the water of 12 times through 8 is added, preferably, White heat hours or 3 in the room temperature, 11 through 8 a pH the strong base such as NaOH potassium hydroxide is increased preferably it agitates with 12 hour or 1, the first step, the second step, 7 tim through the weight ratio 3 in (c) precipitate, and the third step adding the low grade alcohol including the etha times amount, a methanol etc. and preferably suspends, and concentrates the supernate centrifuged after decompression, and the fourth stage after it adds the organic solvent like the hexane of an equivalent to (d) concentrate and it mixes. The first step preferably controls as the pH 10 and stirs and extracts White heat hot hours. The second step after adds rivers and hills like the hydrochloric acid to (b) extract and preferably it cor pH as the pH 3 with 4 through 2, it centrifuges and collects only a precipitate. The fourth stage after it adds th solvent like the hexane of an equivalent to (d) concentrate and it mixes, refines the liquid, and it removes the which is a supernate frozen and dries.
- 27 The extract of grape seed manufacturing method by the water is characterized that when the pH of the extrac is 8 or less after the NaOH addition, the pH of the extraction solvent is controlled over 8.0 since the extractior efficiency of the enzyme inhibitor is remarkably reduced and it extracts.
- 28 Moreover, preferably the grape seed ethanol extraction material of the present invention adds 100% ethanol 1 50 and it stirs and extracts the low grade alcohol of the five-fold of the grape seed weight (kg) which dry it sm. 20 times or the water and these mixed solvents in the room temperature White heat hours or 24 hours. After i the hexane of an equivalent to a concentrate after the keen in the decompression concentration and it mixes, and dries the liquid and it obtains the powder of the brown to remove the hexane layer which is a supernate.
- 29 As described above, so that the obtained extract of grape seed confirm the specificity about an alpha-glucosid alpha amylase (α-amylase) of the spittle engaging in the carbohydrate metabolism, and the alpha amylase (α inhibitory activity of the pancreas were confirmed. Then, an extract showed the specific inhibitory activity abo keratinases and it examined closely in the decrease of blood glucose for the first time that it had an effect.
- 30 This with the enzyme, which an alpha-glucosidase does the action of paying the alpha - glycosidic linkage inc alpha amylase, an isomaltase, a glucoamylase, a sucrase etc.
- 31 The present invention is to provide the composition for the decrease of blood glucose which it has the extract seed which the manufacturing process is manufactured with the manufacturing process as the effective comp does.

32 The present invention is to provide the diabetes which it has the extract of grape seed which the manufacturer process is manufactured with the manufacturing process as the effective component, it does, and the glycemic disease, the obesity prevention and for treating pharmaceutical composition.

33 Additionally, the composition for the decrease of blood glucose and the diabetes, and the glycemic disease, the obesity prevention and for treating pharmaceutical composition containing the extract of grape seed of the present invention include an extract about the total weight of composition to 50 weight% through 0.1.

34 Particularly, as to the glycemic disease, while the diabetes is chronically progressed, a complication including diabetic retinopathy, diabetic neuropathy, nephropathy, atherosclerosis, myocardium failure, skin hindrance, a foot syndrome and peripheral vascular disease etc. is included is the anaplasia complication caused by the diabetes.

35 The composition including the extract of grape seed of the present invention more can include the proper carrier generally the composition including the extract of grape seed of the present invention uses in the Holotrichia (pharmaceutical composition, and an excipient and diluent.

36 The lactose, dextrose, sucrose, sorbitol, mannitol, xylitol, erythritol, maltitol, starch, gum acacia, alginate, gel calcium phosphate, calcium silicate, cellulose, methylcellulose, microcrystalline cellulose, polyvinylpyrrolidone, methylhydroxybenzoate, propyl hydroxy benzoate, talc, magnesium stearate and mineral oil can be given as carrier which can be included in the composition including the extract of the present invention, and an excipient and diluent.

37 According to the respective normal method, the composition including an extract formulates in the form of the dosage form of an acida, granule, refinement, capsule, colloidal suspension, emulsion, syrup, an aerosol etc, external use medicine, and a suppository and sterilization injection solution and the composition including an extract can be used.

38 Moreover, as to the extract of grape seed of the present invention, use is possible as the main part of the other and the supplementary raw material and food addition.

39 Moreover, the present invention is to provide the decrease of blood glucose including the allowable food additive extract of grape seed and sitology, and the health promoting food for the prevention of diabetes or the obesity prevention.

40 The composition including the extract of the present invention can be variously used to the medicine for the prevention of the diabetes or the obesity and treatment, the food and drink etc. There can be for example, all kinds of the foodstuffs, a drink, the chewing gum, a difference, the vitamin composition, the health nutraceuticals etc as adding this extract.

41 A toxicity and side effect are the medicine which the extract itself of the present invention becomes relieved to the purpose of prevention in the long-term dose since nearly doing not have and it can use.

42 The extract of the present invention can be the prevention of an obesity and diabetes added to the food or the drink for a purpose.

43 As to the health beverage composition of the present invention, in the extrinsic containing an extract as the essential ingredient, the special limiting point is not in the liquid component. And it can contain the different kinds flavor agent or the natural carbohydrate etc. like the normal drink as the addition component. The example of the above described natural carbohydrate is a monosaccharide, for example, a disaccharide including the glucose, the fructose etc., the polysaccharide including the maltose, a sucrose etc., a sorbitol and the normal xylitol, a sorbitol, an erythritol etc.

including, the alcohol including the dextrin, a cyclodextrin etc. The natural flavor (thaumatin, and the stevia for example, for example, the lever woodi oside A/6, a glycyrrhizin etc) and artificial flavors (the saccharin, an asp etc) can be used as the flavouring agent except the above-described thing in relatively favorable. Generally p the rate of the natural carbohydrate is 12 g/6 through about 5 with the composition 100 ml of the present inve

44 The composition of the present invention can contain the carbonation agent etc. besides above statement us flavor, the coloring agent and leading figure the (A cheese, the chocolate etc), the pectic acid and of which sa alginic acid and of which salt, organic acid, protective colloid thickening agent, PH adjusting agent, stabilizer, antiseptic, glycerine, alcohol, carbonated drink including the different kinds nutraceutical, vitamin, mineral (etc synthetic flavor and natural flavoring etc. Besides that, the compositions of the present invention can contain for the Holotrichia of the nature fruit juice and fruit juice beverage and vegetable beverage. This component a and this component independently can use in other words. It is general that the rate of this additive is not imp the rate of this additive is like that selected in the range of the composition 100 parts by weight 0 of the prese invention or about 20 parts by weight.

45 The present invention is more circumstantially explained based on the following embodiment. But by this, the invention is not limited.

46 Embodiment 1: the Holotrichia of the extract of grape seed.

47 An extract was obtained with the sampling method for adding the water to the grape seed and controlling a pH extracting. It extracted with moreover, the conventional ethanol extraction method and an extract was obtaine

48 1-1. Grape seed water extracts Holotrichia.

49 After while mixing after adding the water of 10 times amount to the grape seed 1kg which dry it smashed, the being added and controlling a pH as 10, it stirred and extracted in 6 time normal temperature. The hydrochlor (HCl) was added to the obtained extract and after a pH controlled so that 3 become, it centrifuged and the pre 100g was collected. After concentrating the supernate which added the ethanol of the weight ratio 5 times am the obtained precipitate 100g and suspending and centrifuged after decompression, the hexane of an equival added to the concentrate 50g and a supernate was removed and the lower layer solution was frozen and is d the powder 30g of the brown was obtained.

50 1-2. Grape seed ethanol extract production.

51 While after 50% or 100% ethanol of 10 times amount being added to the grape seed 1kg which dry it smashe mixing at the room temperature, extracting with 12 hour and filtering, it concentrated on 1/10 volume after decompression. The hexane of an equivalent was added to the concentrate 50g and a supernate was remove the lower layer solution was frozen and is dried and the powder 30g of the brown was obtained.

52 Embodiment 2: the inhibition activity measurement of the alpha - amylase of the extract of grape seed.

53 In the above preferred embodiment 1, in order that the specificity about the alpha-glucosidase of the obtained seed water extracts and ethanol extraction material were investigated, the inhibitory activity toward the keratin the respective extract was irradiated by using the alpha amylase (the A-amylase, sigma, A-1031, U.S) of the : and the alpha amylase (the A-amylase, sigma, P-1625, U.S) of the pancreas as an enzyme. At this time, aca

the product name : gluco bi, and the Korea bi) were used as the check plot. An acarbose is known that it lowers dinner blood sugar because of suppressing the α - glucosidase with the oral medicinal water hindering the sucrose rising of after dinner blood sugar of the diabetes patient and delaying a fire-extinguishing and absorption of a carbohydrate.

54 Starch (the starch, and the purchase wife) to a substrate and the inhibitory activity about the alpha amylase (Pancreatin α -Amylase) of the alpha amylase (Salivary α -Amylase) of the spittle or the pancreas measured in water or the ethanol extraction material of the grape seed. In the pH 6.8 the enzyme liquid (spittle alpha amylase unit) $500\mu\text{l}$ and extract of grape seed $1\mu\text{g}$ or $5\mu\text{g}$, and 37°C , after after doing with 10 discrimination preincubation (preincubation), 0.5% starch being added and reacting at 37°C with 7 discrimination, DNS (3,5-Dinitrosalicylic) chromogenic agent (sigma, D-0550, and U.S) $500\mu\text{l}$ were put and the reaction was stopped. In 100°C this, after pressing heavy on 15 discrimination and coloring and enough cooling, the water of a treble was added to the solution. And an absorbance was measured in 540nm after well agitating. In this way, the inhibition ratio was calculated from a difference with the value which instead of put the water or the ethanol of an equivalent the ratio obtaining in into the reaction solution with extract and the result was shown for Fig. 1, and 2.

55 Fig. 1 shows the result it is the graph showing the spittle alpha amylase inhibition rate of activity of the acarbose and grape seed water extracts $2.5\mu\text{g}$, and Fig. 2 is the grape seed water extracts $2.5\mu\text{g}$ and the graph and shows the alpha amylase inhibition rate of activity of the pancreas of the acarbose $2.5\mu\text{g}$, and that it irradiates the concentration (IC_{50}) of the extract of grape seed reducing the alpha amylase activity with 50% the diagram below 1.

56 The effect that the extract of grape seed of the present invention hindered the alpha amylase activity of the spittle saw the result of Fig. 1 could know to be excellent than an acarbose. If the result of Fig. 2 was seen, it became the alpha amylase inhibition rate of activity of the pancreas with about 60% and the extract of grape seed suppressed the blood glucose level increase but it confirmed that it had an effect.

57 And in case of the concentration (IC_{50}) result of suppressing the alpha amylase activity of the table 1 with 50% extract of grape seed could confirm to be similar with an acarbose, efficiently hinder the alpha amylase of the pancreas and spittle in the low concentration.

Table 1

Sample	The sample density required for the alpha amylase deactivation (50%) (μg)	
	The alpha amylase of the spittle (α -amylase)	The alpha amylase of the pancreas (α -amylase)
Extract of grape seed	1.62	3.72
Acarbose	2.5	2.5

58 Embodiment 3: the alpha amylase (α -amylase) inhibitory activity of the pancreas and spittle.

59 The concentration of the extract of grape seed was processed as 0, 0.5, 0.67, 1 and $1.25\mu\text{g}$ and the inhibitor was measured to be the inhibition activity measurement method about the alpha amylase (Pancreatin α -Amylase) of the alpha amylase (Salivary α -Amylase) of the spittle or the pancreas in the grape seed water extracts and ethanol extraction material. In this way, the enzyme reaction velocity measured was shown in terms of the Lineweaver

plot and the result showing about the inhibitory activity was shown for Fig. 3, and 4.

60 [S] is the concentration of a substrate. [V] shows the reaction speed.

61 As shown in figs. 3 and figs. 3 in the concentration which is the alpha amylase of the pancreas and spittle low extract confirmed to efficiently obstruct.

62 The extract of the present invention can administer to the following formulation. And the following formulation embodiment exemplifies the present invention. By this, the content of the present invention is not limited.

63 The Holotrichia of the formulation example 1. injectable formulation.

64 The extract 100 mg of the embodiment 1.

65 Sodium metabisulfite 3.0 mg.

66 Methylparaben 0.8 mg.

67 Propylparaben 0.1 mg.

68 Scanning sterilization distilled water proper quantity.

69 After the component described in the above is mixed and the final volume manufactures with the normal mett that 2ml be, it charges to the ample of 2ml capacity and it sterilizes and the injection is made.

70 The Holotrichia of the formulation example 2. refinement.

71 The extract 200 mg of the embodiment 1.

72 Lactose 100 mg.

73 Starch 100 mg.

74 Magnesium stearate dosage.

75 According to the normal refining manufacture method, the component described in the above is mixed and it and a refinement is manufactured.

76 The Holotrichia of the formulation example 3. capsule.

77 The extract 100 mg of the embodiment 1.

78 Lactose 50 mg.

79 Starch 50 mg.

80 Talc 2 mg.

81 Magnesium stearate dosage.

82 According to the normal capsule manufacturing method, the component described in the above is mixed and charges to the gelatine capsule and a capsule is manufactured.

83 The Holotrichia of the formulation example 4. liquor.

84 The extract 1000 mg of the embodiment 1.

85 Oligosaccharide 20 g/6.

86 20g per an isomerization.

87 Lemon flavor dosage.

88 The purified water was added and it fitted with the whole 1000ml.

89 According to the manufacturing method of the normal liquor, after the component described in the above is m charges to the brown bottle and it sterilizes and a liquor is manufactured.

90 The Holotrichia of the formulation example 5. pilule.

91 The extract 100 g/6 of the embodiment 1.

92 Wheat flour 100 g/6.

93 Purified water 500ml.

94 After 100g wheat flour being put in the water of 500ml and heating, it completely mixes, it cools if it is solidifie half. After mixing the complex herb medicine 100g and completely mixing and kneading, it puts into a mould & ventilates and it dries and it manufactures.

95 The Holotrichia of the formulation example 6. mixed liquid medicine.

96 The extract 1000 mg of the embodiment 1.

97 Citric acid 1000 mg.

98 Oligosaccharide 100 g/6.

99 Concentrated liquid of plum 2 g/6.

100 Taurine 1 g/6.

101 Lemon flavor dosage.

102 The whole 100 ml the purified water is added.

103 According to the manufacturing method of the normal liquor, after the component described in the above is m charges to the brown bottle and it sterilizes and a liquor is manufactured.

104 The Holotrichia of the formulation example 7. health promoting food.

105 The extract 1000 mg of the embodiment 1.

106 Vitamin mixture proper quantity.

107 Vitamin A acetate 70 μ g.

108 Vitamin E 1.0 mg.

109 Thiamin 0.13 mg.

110 Vitamin B 0.15 mg.

111 Pyridoxine 0.5 mg.

112 Cyanocobalamin 0.2 μ g.

113 Vitamin C 10 mg.

114 Biotin 10 μ g.

115 Niacin amide 1.7 mg.

116 Folic acid 50 μ g.

117 Calcium pantothenate 0.5 mg.

118 Proper quantity of inorganic matter mixture.

119 Inorganic iron 1.75 mg.

120 Zinc oxide 0.82 mg.

121 Magnesium carbonate 25.3 mg.

122 First potassium phosphate 15 mg.

123 Dibasic calcium phosphate 55 mg.

124 Potassium citrate 90 mg.

125 Calcium carbonate 100 mg.

126 Magnesium chloride 24.8 mg.

127 The composition ratio of the mineral mixture and vitamin described in the above was the component which was suitable for the relative health promoting food the mixed tide under the castle wall to the preferred embodiment. However, it is acceptable even if it arbitrarily transforms the combination ratio and executes. And after the composition ratio of the mineral mixture and vitamin described in the above mixes the component described in the above according to the normal health food production method, it manufactures a granule. It can use according to the normal method of the health promoting food composition manufacture.

128 The Holotrichia of the formulation example 8. health functional beverage.

129 The extract 1000 mg of the embodiment 1.

130 Citric acid 1000 mg.

131 Oligosaccharide 100 g/6.

132 Concentrated liquid of plum 2 g/6.

133 Taurine 1 g/6.

134 The whole 900 ml of the purified water is added.

135 According to the normal health functional beverage manufacturing method, after the component described in the above is mixed, after it stirs and heats in the White heat for hour 85°C, after ***ing after acquiring in 2 ℥ containing filtering the solution and is sterilized and sterilizing with sealing, it uses in the health functional beverage composition manufacture of the present invention.

136 It may be acceptable that the composition ratio was the component which was suitable for the relative favorite beverage the mixed tide under the castle wall to the preferred embodiment. However, it arbitrarily transforms the combination ratio and executes according to the demand hierarchy, the demand country, the local including up to the ethnic preference.

▶ Effects of the Invention

137 As described above, the water extraction method of the grape seed reduces amount of the used organic solvent in comparision with the conventional ethanol extraction method. It is not necessary to have the separate step of And since being extracted to the adjustment of a pH, it is the sampling method economic and simple. Moreover, the extract of grape seed has the excel effect that hinders an alpha-glucosidase and the absorption of the glucose within the blood and suppressing the blood glucose increase after eating, the effect can be very usefully used as a hypoglycemic agent, and the diabetes / Corpulence cure with the biomedical industry phase.

 **Scope of Claims****Claim[1] :**

138 (a) The manufacturing method of the extract of grape seed comprising: the manufacturing process it adds the 12 times through 8 of the grape seed weight (kg) which dry it smashes; it agitates in the room temperature within 1 hour or 1; and of increasing the strong base and controlling a pH as 11 through 8 and being made of the first stirring and extracts White heat hours or 24 hours, the second step, the third step, and the fourth stage; the second step centrifuges after adding rivers and hills to (b) extract and controlling a pH as 4 through 2 and collects only precipitate; the third step adds the ethanol of 7 times through the weight ratio 3 to (c) precipitate and it suspends; concentrates the supernate centrifuged after decompression; and the fourth stage adds the organic solvent or equivalent to (d) concentrate and it mixes; it removes the hexane which is a supernate and it refines the south liquid; and it freezes and dries.

Claim[2] :

142 The manufacturing method of claim 1, wherein the grape seed is selected in the grapes (*Vitis vinifera L.*), the European grape (*Vitis vinifera*), the *Vitis labrusca*, the *Vitis riparia*, the desert pavement (*Vitis rupestris*), the *Vitis berladieri*, the *Vitis coignetiae PULLIAT* (*Vitis coignetiae Pulliat ex Planchon*), the *Vitis amurensis Ruprecht*, the *Vitis ficifolia Bunge* and *Vitis flexuosa THUNB* (*Vitis flexuosa Thunb.*) than over one.

Claim[3] :

143 The composition for the decrease of blood glucose which it has the extract of grape seed in which it has the α -glucosidase inhibitory activity as the effective component, it does.

Claim[4] :

144 The composition which is an extract of claim 3, wherein the extract of grape seed is available in the polar solvents these mixed solvents including the water, a methanol, the ethanol etc.

Claim[5] :

145 The composition of claim 4, wherein the ethanol is 50% or 100% ethanol.

Claim[6] :

146 The composition of claim 3, wherein the grape seed is selected from the grapes (*Vitis vinifera L.*), the European grape (*Vitis vinifera*), the *Vitis labrusca*, the *Vitis riparia*, the desert pavement (*Vitis rupestris*), the *Vitis berladieri*, the *Vitis coignetiae PULLIAT* (*Vitis coignetiae Pulliat ex Planchon*), the *Vitis amurensis Ruprecht*, the *Vitis ficifolia Bunge* and *Vitis flexuosa THUNB* (*Vitis flexuosa Thunb.*).

Claim[7] :

147 The diabetes, the obesity prevention and for treating pharmaceutical composition of any one of claims 3 through 6, wherein the extract of grape seed is contained.

Claim[8] :

148 The health promoting food including the allowable food additive to the extract of grape seed for the decrease glucose or the obesity prevention and sitology.

Claim[9] :

149 The health promoting food of claim 8, wherein it is the health beverage.